REMARKS/ARGUMENTS

This amendment is submitted in response to the Office Action dated July 15th, 2003. After entry of this amendment, claims 1-26 will be pending in the application. Claim 1 has been amended to incorporate language to correct § 112 issues. Claim 1 has further been amended to define over the prior art of record. Reconsideration and allowance is respectfully requested in view of the amendments made and the remarks made below.

The Applicant would like to thank the Examiner for granting the Applicant a personal interview on August 29, 2003.

1. The §112 Second Paragraph Rejections

Claims 1-13 were rejected in the Office Action under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 1 was rejected because step (b) of the claim stated "drying the granulated microcrystalline cellulose at a controlled rate for a time sufficient to remove at least substantially all of the polar organic solvent." It was argued that this was indefinite because pg. 6, first paragraph of the instant specification defined the rate of controlled drying as carrying out the drying step with no more than a minimal input of heat or reduction in pressure for drying. It was argued that the specification does not provide a standard for ascertaining the requisite degree of heat input. The Applicant in response to this argument and as discussed in the interview of August 29, 2003, has amended claim 1 to overcome the 35 U.S.C. §112 rejection by adding the language "with no heat input" and additionally the language "at ambient temperature." Applicant believes that this amendment has removed any 35 U.S.C. §112 issues and earnestly requests the removal of the 35 U.S.C. §112 rejection.

2. The Rejection under § 102(e)

Claims 1, 2, and 4-11 are rejected under 35 U.S.C. §102(e) as being anticipated by Asgharnejad et al. U.S. Pat. No. 6,123,964 (hereinafter "Asgharnejad"). Applicant has amended

claim 1 by adding the language "with no heat input at ambient temperature." There is no teaching in Asgharnejad of drying the granulated microcrystalline cellulose at a controlled rate with no heat input at ambient temperature. For a 35 U.S.C. §102 rejection to stand each and every element of the claim must be met.

Asgharnejad teaches "drying the granules to remove the ethanol/water with heated air in a fluid bed dryer or tray dryer for 10 minutes to 24 hours." See col. 3, lines 4-6. Asgharnejad is using heated air for its drying step. Amended claim 1 provides for "no heat input at ambient temperature." This defines over Asgharnejad, which specifically teaches heating the air. The step of heating the air is specifically excluded in first drying step of the instant invention.

Furthermore, Asgharnejad is only concerned with removing the ethanol/water granulating fluid, and contains no teaching that it is important or desirable to remove the ethanol component of the granulating fluid at a controlled rate, or that a beneficial result could be obtained by removing the ethanol component at a controlled rate. Moreover, despite the fact that Asgharnejad contains a detailed description of the various components that may be included in its tablets, Asgharnejad does not contemplate the use of controlled release particles. Thus, since the formulations of Asgharnejad do not contain controlled release particles, Asgharnejad is not concerned with the goal of the present invention of providing microcrystalline cellulose granules that can provide a cushioning effect to such controlled release particles during a tabletting process.

Asgharnejad exemplifies only a single drying step and this same drying step is employed in Examples 19, 20, 23 and 25 of Asgharnejad. See col. 39, lines 28-30; col. 40, lines 41-43; col. 41, lines 44-46 and col. 42, lines 49-51 of Asgharnejad. The exemplified drying step of Asgharnejad dries the wet granules at 47°C in a tray dryer or a fluid bed dryer for approximately 3.0 hours. This is not the same as the "controlled rate with no heat input at ambient temperature" drying step of claim 1 of the present invention. 47°C is not ambient temperature, and Asgharnejad requires heat input to obtain this drying temperature. This is different than the instant invention where the first drying step is carried out with no heat input.

Asgharnejad therefore does not meet each and every limitation of amended claim 1 and therefore Applicant earnestly request that the 35 U.S.C. §102(e) rejection be removed. The 35

U.S.C. §102(e) rejections of claims 2-13 should be removed by virtue of their dependence upon claim 1.

3. The Rejections under 35 USC § 103(a)

The rejection further rejects claims 1-13 under § 103(a) as being obvious in view of Asgharnejad.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 265 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine,* 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Asgharnejad teaches "drying the granules to remove the ethanol/water with heated air in a fluid bed dryer or tray dryer for 10 minutes to 24 hours." See col. 3, lines 4-6. Asgharnejad is using heated air for its drying step. Amended claim 1 provides for "no heat input at ambient temperature." This defines over Asgharnejad, which specifically teaches heating the air. The instant invention requires a drying step with no heat input at ambient air temperature; also see those arguments made in section 2 above. Therefore, Applicant contends that a *prima facie* case for obviousness is not provided since this feature of amended claim 1 is neither suggested nor taught by Asgharnejad.

Claim 3 has further been rejected under §103(a) as being unpatentable over Asgharnejad in view of Flanner et al. (U.S. Pat. No. 6,384,020 (hereinafter "Flanner")). Claim 3, which was also rejected under § 102 (e), is also rejected under 35 U.S.C. §103 (a). Applicant assumes therefore that the 35 U.S.C. § 102(e) rejection of claim 3 over Asgharnejad taken alone, is incorrect, because the 35 U.S.C. §103(a) rejection states that Asgharnejad does not disclose isopropanol. Applicant further contends that the 35 U.S.C. § 103 rejection based on Flanner is also overcome because Asgharnejad does not disclose the newly amended limitation of having "no heat input at ambient temperature" and Flanner does not cure this deficiency of the Asgharnejad reference. Therefore not all limitations are taught or disclosed in the prior art references and thus the Examiner has not made out a case of *prima facie* obviousness.

Claims 12 and 13 are rejected under § 103(a) as being unpatentable over Asgharnejad in view of Erkoboni et al., U.S. Pat. No. 5,725,886 (hereinafter "Erkoboni"). Claims 12 and 13, which were also rejected under 35 U.S.C. §102 (e), are also rejected under 35 U.S.C. §103 (a). Applicant assumes therefore that the 35 U.S.C. §102(e) rejection of claims 12 and 13 is incorrect, because the 35 U.S.C. §103(a) rejection of claims 12-13 states that Asgharnejad does not disclose the hydrocolloids claimed in claims 12-13. Applicant further contends that the 35 U.S.C. §103(a) rejection based on Erkoboni is also overcome because Asgharnejad does not disclose the newly added limitation of having "no heat input at ambient temperature" and Erkoboni does not cure this deficiency of Asgharnejad. Therefore not all limitations of claims 12-13 are taught or disclosed in the prior art references and thus the Examiner has not made out a case of *prima facie* obviousness.

Claims 14-16, and 18-26 have been rejected under 35 U.S.C. §103(a) as being unpatentable over McTeigue. More specifically, the Examiner took the position that,

> The McTeigue et al patent discloses microcrystalline cellulose particles having a particle size up to about 220 microns with a particle size standard deviation of from about 75 to about 200 microns (see column 1, line 54), and bulk density at about 0.40 grams/cubic centimeters (see column 2, lines 51 and 52), which embraces the microcrystalline cellulose granules of the instant claims.... Although the McTeigue et al patent only discloses the microcrystalline cellulose thereof as having a mean particle size up to 220 microns, the particle size standard deviation of 200 microns that is disclosed in the McTeigue patent does suggests [sic] microcrystalline cellulose particles that have a particle size of at least 250 microns is [sic – are] present in the McTeigue et al patent. It is within the skill of an artisan to screen a desired microcrystalline cellulose particle size... Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant(s) invention to use the microcrystalline cellulose particles of the McTeigue et al patent that have a particle size of 250 microns, in view of the closely related structures and the resulting expectation of similar drug coating properties.

See pages 10-11 of the Office Action.

Claim 14 is directed to porous microcrystalline cellulose granules having a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns, made by the process of claim 1.

McTeigue clearly states that the microcrystalline cellulose has an average particle size of about 160 to about 220 microns.[1] Thus, the range of mean or average particle size disclosed by McTeigue of 160-220 microns, does not overlap with the claimed range of about 250 to about 1500 microns. The Examiner appears to agree with this point when he stated, "Although the McTeigue et al patent only discloses the microcrystalline cellulose thereof as having a mean particle size of up to about 220 microns..."

However, the Examiner took the position that the particle size standard deviation of 200 microns that is disclosed in the McTeigue patent suggests that microcrystalline cellulose particles that have a particle size of at least 250 microns are present in the McTeigue et al patent. This statement, however, is irrelevant to a determination of the obviousness of claim 14 since claim 14 does not require that the particle size of particular microcrystalline crystalline cellulose particles must be at least about 250 microns. Rather, claim 14 requires that the mean particle size of the microcrystalline cellulose must be at least about 250 microns. Thus, the fact that the McTeigue microcrystalline cellulose may contain some individual particles having particle sizes in excess of 250 microns does not render claim 14 obvious because the fact remains that McTeigue clearly discloses that the mean particle size of the microcrystalline cellulose, taken as a whole, should be from 160-220 microns, which is outside the presently claimed range of claim 14. Thus, the microcrystalline cellulose of McTeigue, taken as a whole, has a smaller mean particle size than the microcrystalline cellulose of the present invention and therefore is clearly different.

The Examiner also took the position that it is within the skill of the artisan to adjust the size of the microcrystalline cellulose particles for optimum effectiveness. Even if skilled person were to adjust the size of the microcrystalline cellulose particles of McTeigue for optimum effectiveness, the skilled person would follow the express teachings of McTeigue that the preferred microcrystalline cellulose has a mean particle size of 180 microns, and therefore would use a mean particle size of about 180 microns when optimizing the McTeigue composition. See e.g. col. 2, lines 40-41 and 48-50 of McTeigue. As a result, optimization of the mean particle size of the McTeigue microcrystalline cellulose leads a skilled person further away from the claimed invention, rather than to the claimed invention.

[1] "Mean particle size" and "average particle size" are known to the skilled person as being synonymous.

Moreover, when a skilled person optimizes the mean particle size of the McTeigue microcrystalline cellulose, such optimization would be carried out within the range of mean particle sizes disclosed in McTeigue, i.e. within the range of mean particle sizes of 160-220 microns. A skilled person would not consider mean particle sizes outside this range in for the purpose of optimization since the expectation from the teachings of McTeigue is that mean particle sizes outside the disclosed range would be sub-optimal, since otherwise McTeigue would have included such mean particle sizes within the disclosed operational range.

The Examiner also takes the position that it is within the skill of an artisan to screen a desired microcrystalline cellulose particle size. However, this still does not lead to the present invention since, following the teachings of McTeigue, a skilled person would screen for a desired mean particle size of 160-220 microns and thus would not arrive at the present invention. In addition, there is no teaching, suggestion or motivation whatsoever in McTeigue to employ a larger mean particle size of at least 250 microns and thus the skilled person would have no motivation to screen for a larger mean particle size, as the Examiner suggests, and therefore would not arrive at the present invention.

The Examiner also takes the position that for the claimed product to be patentable, it must be more efficacious or possess new properties. This is legally incorrect since this would only be the case if the Examiner had made out a case of *prima facie* obviousness. However, for the reasons discussed above, the Examiner has not made out a case of *prima facie* obviousness because the Examiner has not identified a motivation found in the McTeigue reference to modify the composition of McTeigue in order to arrive at the composition of the present invention. Thus, it is not legally required that the products of the present invention be more efficacious or possess new properties in order to be patentable since the products are already patentable because the claimed products are not *prima facie* obvious.

Secondly, the Examples of the present application demonstrate that the microcrystalline cellulose of the present invention provide significant, unexpected improvements in the cushioning properties of the product compared to other, similar products. Examples 1-2 of the present invention each produced tablets with acceptable cushioning properties, whereas Comparative Examples B-C, produced tablets that were too dense to provide adequate

cushioning properties. These examples tend to show that there is, in fact, a significant, unexpected difference between products of the present invention, and similar prior art products.

Finally, the Examiner takes the position that there is an expectation from McTeigue that the McTeigue products would produce similar drug coating properties. The key property of the products of the present invention is cushioning of controlled release particles during tabletting. McTeigue does not set forth a similar utility for its microcrystalline cellulose, i.e. for cushioning controlled release particles during the tabletting process to help preserve their controlled release characteristics. In fact, a close reading of McTeigue demonstrates that the microcrystalline cellulose of McTeigue is used for a totally different purpose than the microcrystalline cellulose of the present invention.

More specifically, McTeigue clearly teaches that,

> The present invention is directed to a particle which comprises a seed core comprised primarily of microcrystalline cellulose, ... to which a pharmaceutically active ingredient in solution is layered onto the microcrystalline cellulose by spray coating.

See col. 1, lines 40-45 of McTeigue. Thus, in the McTeigue pharmaceutical composition, the microcrystalline cellulose forms a seed core and the pharmaceutically active ingredient is spray coated onto the microcrystalline cellulose. In contrast, the utility of the granules of the present invention is in pharmaceutical compositions wherein the pharmaceutically active ingredient is included in controlled release particles and the controlled release particles and microcrystalline cellulose granules are formed into a tablet by tabletting them together under high pressure. See e.g. page 3, line 21 to page 4, line 9 of the specification. As a result, there is no disclosure in McTeigue that the microcrystalline cellulose of McTeigue needs to have certain properties sufficient to provide cushioning of controlled release granules during a tabletting operation or that the McTeigue microcrystalline cellulose would even be useful in tablets containing controlled release granules.

Therefore, the Examiner has not set forth a *prima facie* case of obviousness against claim 14 of the present application. Claims 15-16 and 18-26 depend, directly or indirectly, from claim 14. Because claim 14 is not obvious over McTeigue for the reasons given above, it

follows by statute that claims 15-16, and 18-26 are also not obvious over McTeigue for at least the same reasons.

Claim 17 has been rejected under 35 U.S.C. §103(a) as being unpatentable over McTeigue in view of U.S. Patent no. 6,117,451 (Kumar). This rejection is traversed for the same reasons as the rejection of claim 14, namely, that neither McTeigue nor Kumar teaches or suggests that the microcrystalline cellulose should have a mean particle size of 250-1500 microns. Favorable consideration and withdrawal of the rejection is requested.

3. Conclusion

Applicant has made an earnest effort to place this application in condition for allowance. If the Examiner feels that a telephone interview would expedite prosecution of this patent application, he is respectfully invited to telephone the undersigned at 215-599-0600.

Respectfully submitted,

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